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ELEVATED PLASMA MARINOBUFAGENIN, AN ENDOGENOUS CARDIOTONIC STEROID, IS ASSOCIATED WITH RIGHT VENTRICULAR DYSFUNCTION AND NITRATIVE STRESS IN HEART FAILURE

Moderated Poster Contributions
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Background: Plasma levels of cardiotonic steroids are elevated in volume-expanded states such as chronic kidney disease and preeclampsia, but the role of these salt-sensitive natriuretic hormones in heart failure (HF) is unclear. We investigated the determinants of systemic levels of marinobufagenin (MBG) in HF, and its association with long-term outcomes and nitrative stress.

Methods: We first measured plasma MBG levels and performed comprehensive clinical, laboratory, and echocardiographic assessment in 245 HF patients. All-cause mortality, cardiac transplantation, and HF hospitalization were tracked for 5 years.

Results: In our study cohort, median [interquartile range] MGB was 583 [383-812] pM. Higher MBG was associated with higher myeloperoxidase (MPO, r=0.42, p<0.0001), NT-proBNP (r=0.25, p=0.001), and asymmetric dimethylarginine (ADMA, r=0.32, p=0.001). Elevated levels of MBG were associated with measures of worse right ventricular function (RV s': r= -0.39, p<0.0001) and are associated with increased risk of adverse clinical outcomes (MBG ≥574 pM: HR 1.58 [1.10-2.31], p=0.014) even after adjustment for age, gender, and left ventricular systolic function. In mice, a left anterior descending coronary artery ligation model of heart failure lead to increases in MBG, while infusion of MBG into mice for 4 weeks lead to significant increases in MPO, ADMA, and cardiac fibrosis.

Conclusion: In the setting of heart failure, elevated plasma levels of MBG are associated with right ventricular dysfunction and are associated with worse long-term clinical outcomes in multivariable models adjusting for established risk factors. Infusion of MBG appears to directly contribute to increased nitrative stress and cardiac fibrosis.